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Björkman, M.

2019

Björkman , M , Jyväkorpi , S K , Strandberg , T E , Pitkälä , K H & Tilvis , R S 2019 , '
Sarcopenia Indicators as Predictors of Functional Decline and Need for Care among Older
People. ' , Journal of nutrition, health & aging , vol. 23 , no. 10 , pp. 916-922 . https://doi.org/10.1007/s12603-019-128

http://hdl.handle.net/10138/323900
https://doi.org/10.1007/s12603-019-1280-0

publishedVersion

J Nutr Health Aging. 2019;23(10):916-922

SARCOPENIA INDICATORS AS PREDICTORS OF FUNCTIONAL DECLINE AND NEED FOR CARE AMONG OLDER PEOPLE

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Abstract: *Objectives:* Sarcopenia is associated with poor health outcomes. We examined the relative roles of muscle mass, strength, physical performance and obesity as health predictors among older sarcopenic people. *Design and participants:* This prospective study examined community-dwelling people aged 75+ (N=262). *Setting:* Porvoo Sarcopenia and Nutrition Trial. *Measurements:* We collected demographic data and medical history by postal questionnaire including RAND-36 at baseline and at four years and measured BMI, Short Physical Performace Battery (SPPB), hand-grip strength, cognition and two surrogate measures of muscle mass; the Single Frequency Skeletal Muscle Index (SF-SMI) and the Calf Intracellular Resistance Skeletal Muscle Index (CRi-SMI). *Results:* Adjusted for age and gender, independent outdoors mobility was predicted positively by baseline physical functioning scores in RAND-36 ($p<0.001$), the SPPB ($p<0.001$), the two-minute step test ($p<0.001$), and grip strength ($p=0.023$), as well as CRi-SMI ($p<0.001$). However, the prediction was negative in BMI ($p<0.001$) and the Charlson co-morbidity Index ($p= 0.004$). Similar associations were found when the physical component RAND-36 was used as an outcome measure. The use of home care was predicted by high co-morbidity ($p=0.057$) and low scores in RAND-36 ($p<0.001$), SPPB ($p<0.001$) and the two-minute step test ($p<0.001$), and low CRi-SMI ($p< 0.001$). CRi-SF was a more consistent predictor than SF-SMI, which was partly masked by BMI. Controlled for age, gender and comorbidity, a 10% difference in CRi-SMI was associated with a 4% higher probability ($p=0.019$) of independently living at home, whereas the respective figures for SF-SMI and BMI were -18% ($p=0.098$) and -14% ($p=0.088$). *Conclusions:* In contrast to SF-SMI, high CRi-SMI appeared to indicate good prognosis and less need of care, independently of BMI.

Key words: Sarcopenia, muscle mass, muscle strength, activities of daily living, Bioimpedance analysis.

Introduction

Sarcopenia as a clinical syndrome has been described as low muscle strength and/or low muscle quality or quantity and poor physical performance (1-3). Depending on the definition, the prevalence of sarcopenia is reported to be up to 29% among older community-dwelling adults and up to 33% among individuals living in long-term care institutions (1-3). Several studies have linked sarcopenia as a clinical entity to morbidity and mortality, impaired physical disability, falls, fractures, poor quality of life, depression and hospitalization (4-11). In a recent review, sarcopenia, defined by computed tomography, was common among chronically ill hospital patients and associated with infectious complications, longer hospitalization, higher mortality and greater need for rehabilitation (12).

The relative role of various sarcopenic components as health predictors has raised discussion and clearly needs further evaluation. Special attention has been paid to the comparative importance of muscle loss and muscle function. Although both low muscle mass and poor muscle function predispose older adults to poor health outcomes, the associations of their components with aging differ (13, 14). Several studies have shown that mid-arm muscle and calf circumferences correlate with appendicular muscle mass and reflect both health and nutritional status and predict physical performance, health and survival among older people (7, 8, 15, 16). Clark and Manini have emphasized that the loss of muscle function represents a greater risk of poor health outcomes and physical dependence than the loss of muscle mass and that monitoring muscle strength has greater feasibility in everyday practice (17). Some studies suggest that muscle function may be a more powerful predictor of disability and mortality than muscle mass (18,19) and that reduced muscle quality has a greater impact on physical independence (13, 20, 21). A recent, large cross-sectional study associated low muscle mass with a risk of losing physical independence at 90 years of age, but the loss of muscle function played a more dominant role, and the presence of both criteria presented the greatest risk (22).

Simultaneous obesity or lack of obesity has also often confounded results. For instance, it has been suggested that obesity combined with poor muscle function, but not with low muscle mass, predicts the risk of falls at older ages (23). According to a review of 12 prospective cohort studies, sarcopenic obesity was associated with a 24% increased risk of all-cause mortality (24). However, in a recent English study, sarcopenic obesity did not confer any greater risk than sarcopenia alone (25). The greatest mortality was observed when sarcopenia was associated with weight loss.

Most characteristics of sarcopenia are relatively easy to measure and standardize. However, obtaining an accurate measure of muscle mass may be a major obstacle. Magnetic resonance imaging (MRI), computed tomography (CT) and

Received March 24, 2019
Accepted for publication April 8, 2019

Published online October 12, 2019, http://dx.doi.org/10.1007/s12603-019-1280-0

dual energy x-ray absorptiometry (DXA) are not often available for large-scale population studies (1). Transportable bio-electrical impedance analysis (BIA) estimates the volume of fat and lean body mass based on the relationship between the volume of a conductor and its electrical resistance. The method is not expensive, requires no specialized staff and is relatively easy to use in clinical practice, both on ambulatory subjects and hospitalized patients. Although the accuracy of the method has been criticized because it has been reported to overestimate muscle mass and underestimate fat mass (26-30), it can provide valid measurements (31). Bioimpedance spectroscopy (BIS) uses hundreds of frequencies within a wide range, allowing the calculation of intracellular resistance (Ri), a measure that does not require data on subject characteristics or population-based algorithms. Ri is closely related to the intracellular water (ICW) compartment and may be considered a surrogate for skeletal muscle cell mass, as fat and bone cells have low intracellular water content (26).

In order to obtain a deeper insight into the relative influences of sarcopenia indicators, it seems to be justifiable to simultaneously and repeatedly test all the characteristics of sarcopenia longitudinally, in sufficiently long-term studies with a large series of independent outcomes. For this purpose, we related measures of muscle mass, muscle strength, and physical functioning indices registered three times during the first year to the outcome four years later. We placed special emphasis on the predictive value of two bioimpedance measures of muscle biology.

Methods

Participants

The data were derived from the Porvoo Sarcopenia and Nutrition Trial (ACTRN12612001253897) (32). Briefly, we approached the 75+ population living in Porvoo, Finland (N=3275) via a postal questionnaire (response rate 60.5%), and the research group further examined the individuals at risk of sarcopenia (limitations in activities of daily living, sedentary lifestyle, falls, exhaustion, old age, low BMI) (N= 428). Of these, 88 died within four years. A total of 182 randomized people participated in a three-armed, 12-month intervention trial and were re-examined at six months and at one year from baseline. Of these participants, 33 died before the four-year examination. We obtained the census status and date of death of the participants from the bureau of Official Statistics of Finland (SVT) in 2016, which is 100% complete.

Data collection and examinations

We collected demographic data and medical history by postal questionnaire at baseline and at four years. The response rate for the four-year postal questionnaire was 79.1% (N=262/340). The questionnaires included a Finnish translation of the physical functioning RAND-36 (0–100 points) (33). Morbidity was classified according to the Charlson Comorbidity Index (CCI) (34).

The participants at risk of sarcopenia were examined clinically at a day clinic or during a home visit. We assessed physical performance using the short physical performance battery (SPPB) (35), with 0 points indicating poorest and 12 best performance. The tests included measurements of walking speed (36) and the chair-stand-test (37). Muscle strength was assessed using a hand grip dynamometer (JAMAR dynamometer, Saehan Corp., Masan, Korea). Cognitive function was evaluated by the Minimental State Examination (MMSE) (38), muscle endurance by the two-minute step test (39), and BMI was also calculated.

Bioimpedance spectroscopy was performed using a single-channel, tetra polar device (SFB7, ImpediMed Ltd., Eight Miles Plains, Queensland, Australia) that scans 256 frequencies between 4 and 1000 kHz. We recorded the values without further software processing. Segmental calf intracellular resistance skeletal muscle index (CRi-SMI) was calculated from the BIS data of calf measurements as follows: CRi-SMI=electrode distance2/Ricalf (cm2/Ω), using the means of both calves. The whole-body single frequency skeletal muscle index (SF-SMI) was calculated from the whole-body skeletal muscle mass (SMM), assessed according to Janssen et al. [40]. It was then transformed into the skeletal muscle index as follows: SF-SMI=SMM/height^2.

The survey elicited the use of home-care services.

Ethics

The study protocol was approved by the ethics committee for internal medicine of the hospital district of Helsinki and Uusimaa. We obtained informed consent from each patient or their next of kin. The participants signed their informed consent before the start of any trial procedures. In the case of a participants' cognitive decline ((MMSE) <19) (38) or poor capability of judgment, a proxy was invited to give consent in addition to the participant's consent.

Statistics

We used SPSS software (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) for the statistical analyses. Continuous variables with normal distribution were expressed by means with standard deviations (SD) and those with skewed distribution by medians with first and fourth quartile cut-off points. For the variables with normal distribution, we conducted statistical comparisons of the groups using Student's t-test, and for those with skewed distribution the Mann-Whitney U test. When appropriate, we used analysis of variance. The Chi-Square test was used to test the relationship between the two categorical variables and Fischer's exact test was used when appropriate. We performed binary logistic regression analysis and linear regression analyses to assess the prognostic significance separately for each test variable. Age and gender were used as covariates.

Table 1
Baseline characteristics (SD) of participants of follow-up study (N=262) by gender and use of home care services at four years

Variable	Women (N=194)	Men (N=68)	P-value
Mean age (SD), years	82.4 (4.4)	83.4 (4.5)	0.248
Mean Charlson Comorbity Index (SD)	1.76 (1.6)	2.22 (1.5)	0.037
BMI, kg/m^2	27.4 (4.6)	27.3 (4.2)	0.491
SPPB (0-12)	9.01 (2.4)	8.9 (3.0)	0.649
RAND-36 (0-100)	53.3 (29.2)	57.7 (29.6)	0.257
Walking speed, m/s	0.95 (0.23)	0.95 (0.30)	0.984
Two-minute step test, no	80.2 (22.5)	82.7 (23.4)	0.480
Grip strength, kg	18.3 (4.1)	28.0 (7.0)	<0.001
SF-SMI, kg/m2	6.94 (0.91)	9.79 (1.09)	0.060
CRi-SMI, cm2/Ω	1.14 (0.38)	1.76 (0.51)	<0.001
	Non-user (N=153)	**User (N=109)**	**P-value**
Age, years	81.8 (4.7)	84.4 (4.7)	<0.001
Mean Charlson Comorbity Index (SD)	1.75 (1.5)	2.14 (1.7)	0.053
BMI, kg/m	27.5 (4.6)	27.2 (4.4)	0.647
RAND-36 (0-100)	62.4 (24.8)	43.2 (26.3)	<0.001
SPPB (0-12)	9.7 (2.2)	8.0 (2.7)	<0.001
Two-minute step test, no	88.3 (24.4)	72.9 (22.6)	<0.001
Grip strength, kg	20.9 (5.7)	20.6 (7.7)	0.713
MMSE (0-30)	26.2 (2.7)	25.9 (2.7)	0.362
SF-SMI, kg/m^2	7.6 (1.5)	7.7 (1.7)	0.663
CRi-SMI, cm2/Ω	1.58 (0.42)	1.39 (0.44)	<0.001
Charlson Comorbidity Index (SD)	1.75 (1.5)	2.14 (1.7)	0.053
BMI, kg/m	27.5 (4.6)	27.2 (4.4)	0.647
RAND-36 (0-100)	62.4 (24.8)	43.2 (26.3)	<0.001

Tähän pitäisi laittaa variaabeleiden referenssit + statist. testit

Results

Baseline characteristics

Of the 428 participants clinically examined at entry, 88 died during the follow-up period. The mean age of the respondents was 83 years at entry. At four years, we sent a postal questionnaire to 340 survivors, which was returned by 262 (79.1%). Compared with the women, the men had more diseases (higher comorbidity index) but greater muscle mass and strength (Table 1). Otherwise, the differences in age, BMI and physical functioning between the genders were insignificant.

Compared with the respondents, the non-respondents (N=78) were sicker (CCI 2.32 vs 1.88, p=0.048), and had poorer performance (SPPB 7.81 vs 8.97, p<0.001), and but their muscle mass SF-SMI (8.16 kg/m^2 vs 7.67 kg/m^2, p=0.022) was higher at baseline. These differences were mainly due to men being over-presented among the non-respondents (30.0% vs 20.1%, p=0.054).

Follow-up

The majority (N=252, 96%) of the participants still lived at home and 153 people (58.4%) did not use home care services at four years (Table 1). Three out of four (72.1%) complained of memory decline. Most (N=185, 70.6%) did not use walking aids indoors and one in two (51.5%) were able to walk outdoors without aids or help. A total of 32 (12%) people were not able to get up from a chair without assistance (hands or other person) and 17 (7%) did not walk outdoors at all. Of the respondents, 98 (37%) had fallen and 15 (6%) had suffered a bone fracture during the previous year. Fifty-eight (22%) reported a weight loss of at least 3 kg during the previous three months but only 26 (10%) regarded their general health as poor.

Table 2
Age- and gender-adjusted predictors of good outdoor mobility (no aids and no help)

Variable	OR	95% CIs	P-value
BMI, kg/m^2	0.88	0.83 – 0.94	<0.001
Baseline RAND-36 (0-100)	1.05	1.04 – 1.06	<0.001
Charlson comorbidity Index	0.76	0.63 - 0.92	0.004
SPPB (1-12)	1.67	1.43 – 1.97	<0.001
Two-min step test. no	1.03	1.02 – 1.04	<0.001
Grip strength. kg	1.07	1.01 – 1.13	0.023
SF-SMI, kg/m^2	0.74	0.55 – 0.98	0.036
CRi-SMI, cm2/Ω	2.40	1.16 – 5.01	0.009

Age and gender were forced into logistic regression analysis as covariates.

Table 3
Test variables measured during one year as age- and gender-adjusted predictors of RAND-36 index four years later

Variable		Standardized beta	95%CI for beta	P-Value
Charlson comorbidity index	Baseline	-0.10	-2.23 -0.09	0.034
SPPS (0-12)	Baseline	0.33	1.73 – 3.14	<0.001
	6 months	0.26	1.85 – 3.84	<0.001
	12 months	0.288	2.11 – 4.04	<0.001
BMI, kg/m^2	Baseline	-0.21	-2.05 -0.60	<0.001
	6 months	-0.17	-2.36 -0.04	0.043
	12 months	-0.15	-2.24 - 0.10	0.072
Two-minute step test. no	Baseline	0.34	0.26 – 0.39	<0.001
	6 months	0.22	0.17 – 0.41	<0.001
	12 months	0.23	0.18 – 0.42	<0.001
Grip strength. kg	Baseline	0.16	0.09 – 0.88	0.016
	6 months	0.19	-0.08 – 2.07	0.070
	12 months	0.24	0.11 – 2.10	0.014
SF-SMI, kg/m2	Baseline	-0.22	-7.46 - -0.51	0.025
	6 months	-0.20	-9.66 – 2.27	0.222
	12 months	-0.32	-11.62 - -0.17	0.044
CRi-SMI, cm2/Ω	Baseline	0.08	-3.25 – 13.72	0.226
	6 months	0.08	-9.35 – 22.67	0.412
	12 months	0.04	-12.68 – 19.71	0.668

Age and gender were forced into linear regression analysis as covariates.

Predictors of physical functioning

Those living independently at four years had lower baseline BMI (26.9 vs 29.3, gender adjusted p = 0.029), and lower SF-SMI (7.53 kg/m^2 vs 7.96 kg/m^2, p = 0.039) but higher CRi-SMI (1.56 cm2/Ω vs 1.38 cm2/Ω, p = 0.010) than the other participants.

The predictive value of the various sarcopenia indicators was first tested in relation to outdoor mobility. Table 2 shows that good physical functioning according to RAND-36, good physical performance according to SPPB, and good walking speed and muscle strength at baseline predicted good outdoor mobility in the follow-up, and that obesity and comorbidity had opposite relationships. The muscle mass indicators showed different results: CRi-SMI was a strong predictor of good

Table 4
Age- and gender-adjusted predictors of use of home care services

Variable	OR	95% CIs	P-value
Baseline RAND-36 (0-100)	0.97	0.96 –0.98	<0.001
Charlson comorbidity Index	1.17	0.99 – 1.38	0.057
SPPB (1-12)	0.79	0.70 – 0.88	<0.001
Two-minute step test. no	0.98	0.97 – 0.99	<0.001
CRi-SMI, cm^2/Ω	0.37	0.18 – 0.74	<0.001

Age and gender were forced into logistic regression analysis as covariates.

Table 5
Comparison of BMI and skeletal muscle indices as predictors of physical functioning at four-year follow-up

Variable	At home without helps[a]			Physical functioning of RAND-36[b]		
	OR	95% CIs	P-value	Standardized beta	95%CI for beta	P-value
			Unadjusted			
BMI, kg/m^2	0.94	0.88 - 0.99	0.031	-0.21	-2.09 -0.56	<0.001
SF-SMI, kg/m^2	0.84	0.71- 0.99	0.045	-0.03	-2.88 – 1.62	0.584
CRi-SMI, cm^2/Ω	2.52	1.32 – 4.83	0.005	0.16	2.33 – 18.9	0.011
			Adjusted for age and gender			
BMI, kg/m^2	0.93	0.88 – 0.99	0.025	-0.20	-2.01 -0.56	<0.001
SF-SMI	0.74	0.55 – 0.98	0.036	-0.21	-7.31 - -9.38	0.030
CRi-SMI, cm^2/Ω	2.41	1.16 – 5.01	0.019	0.07	-4.10 – 13.01	0.306
			Adjusted for age, gender and comorbidity			
BMI, kg/m^2	0.95	0.89 – 1.01	0.088	-0.18	-1.86 - -0.39	0.003
SF-SMI, kg/m^2	0.79	0.058 – 1.05	0.098	-0.17	-6.61 – 0.37	0.079
CRi-SMI, cm^2/Ω	2.43	1.16 – 5.13	0.019	0.07	-4.11 – 12.77	0.314
			Adjusted for age, gender, comorbidity and BMI			
SF-SMI, kg/m^2	0.86	0.60 – 1.24	0.412	-0.01	-4.37 – 4.10	0.951
CRi-SMI, cm^2/Ω	3.47	1.55 – 7.76	0.002	0.15	1.07-18.63	0.028

a. Binary logistic regression analysis. b. Linear regression analysis.

outdoor mobility (OR = 2.40), whereas the association with SF-SMI was significantly negative (OR = 0.74, p = 0.036). When these measures were further adjusted for BMI, the predictive value of SF-SMI was 0.84 (p = 0.34) and that of CRi-SMI rose to 3.62 (p < 0.001) (Table 2).

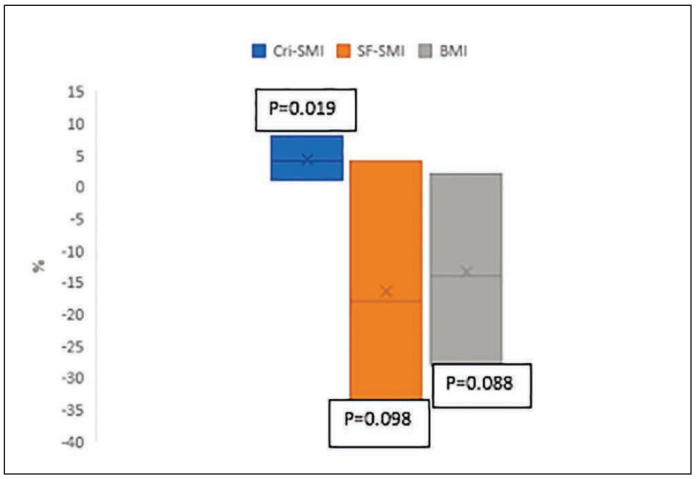
We then tested the associations between potential baseline predictors and the physical component of RAND-36 at four years. We used age and gender as confounders in the linear regression analysis (Table 3). Again, good physical functioning was predicted by higher baseline SPPB, faster walking speed, and stronger hand grip, whereas higher BMI and higher muscle mass according to SF-SMI were associated with lower RAND-36 scores. We found no association between baseline CRi-SMI and RAND-36 score at four years. However, when the effects of muscle mass indices were further adjusted for BMI, the negative predictive values of SF-SMI disappeared, and those of CRi-SMI became positive (standardized beta = 0.18, p = 0.011). The results were consistent for all three measurements during one year. (Table 3)

Use of services

At four years, 69 (26%) people (33 men and 36 women) regularly used either municipal or private home care services. These users were older, had more diseases and reported poorer physical functioning than the non-users. Neither the grip strength nor the muscle mass indictor SF-SMI of the groups differed, but CRi-SMI was lower among the users than the non-users. The significance of the differing characteristics was tested more closely using binary logistic regression analysis, which used age and gender as covariates (Table 4). Again,

the indicators of good physical functioning and performance (RAND-36, SPPB) and good mobility retained highly significant predictive value. This also held true for CRi-SMI.

Figure 1
Probability of independently living at home by 10% differences in muscle mass indices (CRI-SMI and SF-SMI) and body mass index (BMI). The data are adjusted for age, gender and comorbidity



Comparison of BMI and skeletal muscle indices

Finally, we compared the predictive values of BMI and two skeletal muscle indices in relation to the use of help and physical functioning (Table 5). Again, both BMI and SF-SMI were negatively associated and CRi-SMI positively associated with the prognosis of physical functioning according to RAND-36. When adjusted for age, gender and comorbidity, the negative influence of BMI remained virtually unchanged, but the positive association with CRi-SMI accentuated. The latter was also highly predicted after further controlling for BMI. Due to the large differences in the scales of BMI and muscle mass measures, we used percentage distributions (mean =100) for further comparisons (Fig. 1). When controlled for age, gender and comorbidity, a 10% difference in Cri-SMI was associated with a 4% better probability of independently living at home, whereas the respective figures for SF-SMI and BMI were -18% and -14%.

Discussion

This longitudinal study shows that good baseline physical performance and functioning, stronger hand grip strength, higher muscle mass indices and lower BMI predict better physical performance and the need for care of older people at risk of sarcopenia. We also found interesting differences in the predictive significance of various methods in the assessment of muscle mass.

The results do not challenge earlier observations concerning obesity or hand grip strength (41) but provide new insights into the differences of the two muscle mass indices and their interplay with BMI. Both high BMI and high SF-SMI predicted consistently poorer outcomes, whereas high CRi-SMI was associated with good mobility and physical functioning and predicted independent living at home. In this respect, the contradictory results of CRi-SMI and SF-SMI deserve special attention. Closer analyses revealed a relatively strong positive correlation between BMI and SF-SMI (age- and gender adjusted rho = 0.573, $p < 0.001$) at baseline (unpublished data). Thus, the clearly negative influence of high BMI overruns the possible beneficial effects of whole-body muscle mass measured by SF-SMI in this population sample. This was, in fact, verified by adjusting the effects of muscle mass indices for BMI, which partly abolished the negative associations of SF-SMI and accentuated the positive associations of CRi-SMI. The observation that high BMI and low CRi-SMI were both strong, independent predictors of poor physical functioning in old age accord well with the concept of sarcopenic obesity, which has become increasingly important in the aging population (24, 25, 42). Evidence is also increasing that sarcopenic obesity is also associated more with mortality and cardiovascular risk factors than with sarcopenia or obesity alone (24, 26, 44).

The study clearly showed the superiority of CRi-SMI over SF-SMI as a positive mobility predictor among older people. This observation is not surprising, as the former measures the muscle mass of the lower limbs, whereas the latter reflects whole-body muscle mass. It is conceivable that the lower-limb muscles are more important for mobility than whole-body muscle mass. The present results accord well with earlier observations that have shown close associations between Cri-SMI and the daily living activities and mobility of typical nursing home residents (44). Our observations also support the criticism of the validity of SF-SMI measurements of older people (26-30).

The representativeness of the population sample, the serial measures of the key indicators, the clear end-points and the consistency of the results are this study's major strengths. Its weaknesses are its lacking DEXA or MRI measurements.

Conclusion Lower limb CRi-SMI is an independent long-term predictor of the outdoor mobility and physical functioning of older sarcopenic home-dwelling people, whereas the predictive value remains insignificant for whole-body muscle mass index (SF-SMI), which is partly masked by negative influences of high BMI.

Acknowledgements: This study is funded by the University of Helsinki, Konung Gustav V:s och Drottning Victorias Frimurarestiftelse, the Yrjö Jahnsson Foundation, and Valio Ltd. The co-operation of Porvoo municipal health care services is greatly appreciated.

Conflicts of interest: Dr Mikko Björkman reports professional cooperation including lecturing fees from Valio Ltd, Nestle Health Science Ltd. and Nutricia Medical Ltd., Dr Timo Strandberg reports having various educational and consultative cooperation with several companies, including Nutricia, Abbott, Amgen, Merck, Pfizer, Novartis, and Novo-Nordisk; a minor amount of stock in Orion Pharma; and is a board member and former president of executive board of European Union Geriatric Medicine Society which has cooperation also with the nutrition industry. Drs Satu Jyväkorpi, Kaisu Pitkala and Dr Reijo Tilvis have no competing interests.

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